

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)  
(PCT Article 36 and Rule 70)

REC'D 22 FEB 2005

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Applicant's or agent's file reference 205323385	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/AU2004/000337</b>	International filing date ( <i>day/month/year</i> ) 18 March 2004	Priority date ( <i>day/month/year</i> ) 19 March 2003
International Patent Classification (IPC) or national classification and IPC  Int. Cl. <sup>7</sup> A01K 67/027, C12N 15/12		
Applicant  VICTOR CHANG CARDIAC RESEARCH INSTITUTE LIMITED et al		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p style="margin-left: 20px;">a. <input type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of     sheets, as follows:</p> <div style="margin-left: 40px;"> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> </div> <p style="margin-left: 20px;">b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s))     , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							

Date of submission of the demand 15 October 2004	Date of completion of the report 15 February 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  <b>JAMIE TURNER</b> Telephone No. (02) 6283 2071

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AU2004/000337

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1 (b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
  - ☒ the international application as originally filed/furnished
  - ☐ the description:
 

pages	as originally filed/furnished	
pages*	received by this Authority on	with the letter of
pages*	received by this Authority on	with the letter of
  - ☐ the claims:
 

pages	as originally filed/furnished	
pages*	as amended (together with any statement) under Article 19	
pages*	received by this Authority on	with the letter of
pages*	received by this Authority on	with the letter of
  - ☐ the drawings:
 

pages	as originally filed/furnished	
pages*	received by this Authority on	with the letter of
pages*	received by this Authority on	with the letter of
  - ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
  - ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to the sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to the sequence listing (*specify*):

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AU2004/000337

**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims 1-15	YES
	Claims	NO
Inventive step (IS)	Claims 1-15	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-15	YES
	Claims	NO

## 2. Citations and explanations (Rule 70.7)

The following citations, first raised in the corresponding International Search Report, are referred to as follows:

- D1 – Human Molecular Genetics, 2003, 12(6), 601-615
- D2 – Development and Disease, 2002, 129, 3505-2512
- D3 – Biochemical and Biophysical Research Communications, 2001, 286, 478-483
- D4 – Gene, 2001, 274, 217-226

The invention defined by the claims of the international application relates to a zebrafish strain having a dystrophin mutant phenotype resulting from a mutation within the zebrafish dystrophin gene. The invention further relates to a method for screening for agents having potential activity on muscular dystrophy or cardiomyopathy comprising exposing a zebrafish of the strain to candidate agent and determining any affect of the agent on a genetic or physical characteristic of the zebrafish or its progeny. The invention also pertains to a method for monitoring or testing the effect of an agent having activity on muscular dystrophy or cardiomyopathy comprising exposing a zebrafish of the strain to an agent and monitoring the effect of the agent on a genetic or physical characteristic of the zebrafish or its progeny.

Clearly, each of D1-D4 is relevant to the present invention. However, none of D1-D4 actually pertains to a strain of zebrafish which has a mutation in the dystrophin gene. Hence, the claims of the present invention must be considered novel. Further, it is apparent that the skilled person would not, in the light of the teachings of these documents, produce a zebrafish strain having a mutation in the dystrophin gene resulting in the particular phenotype seen in those described in the present application.

D1 discloses juvenile zebrafish whose dystrophin expression was down-regulated (using anti-sense morpholinos) resulting in brain necrosis and other abnormalities (such as curvature). The phenotype described in D1 differs markedly from that described in the present application and would appear to be the result of syndromic affects of morpholino toxicity. D1 does not teach the phenotype produced by a null mutation in the dystrophin gene. The skilled person could not, therefore, predict the phenotype of a zebrafish strain having a mutant dystrophin gene from D1. Hence, D1 would not lead the skilled person to produce the mutant zebrafish of the present application.

D2 discloses the use of anti-sense morpholino oligonucleotides to disrupt the translation of dystroglycan, a protein which interacts with dystrophin, resulting in zebrafish with a phenotype similar to human muscular dystrophy. D2, like D1, results in a phenotype dissimilar to those seen in the present application and would appear to be of a myopathic, rather than a dystrophic, nature. D2 does not predict the phenotype of a zebrafish dystrophin mutation and the skilled person could not predict it from D2. Further, nothing in D2 would lead the skilled person to move from using Dystroglycan morpholino in a suppressor screen to preparing a null zebrafish dystrophin mutant.

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V

Finally, Dystroglycan does not appear to be mutated in any known human muscular dystrophy.

D3 relates to the identification of the zebrafish orthologue of human DMD. D3 suggests that "the zebrafish may prove to be a beneficial vertebrate model to examine the role and functional interactions of dystrophin in disease and development". However, it is apparent that there is insufficient functional evidence to actually support this statement. Hence, the skilled person would not necessarily be lead to do so.

D4 describes the isolation and characterisation of two cDNA clones encoding homologues of dystrophin and a shorter transcript, Dp71, in zebrafish as well as the localisation of the gene on the zebrafish genome. D4 would not lead the skilled person to the dystrophin mutant zebrafish strain as claimed in the present invention.

Hence documents D1-D4 are not prejudicial to the inventive step of claims 1-15 of the present application.